

REMARKS

- A. The claims are fully supported by and are entitled to Applicants' priority claim to U.S. provisional application Serial No. 60/203,151 under 35 U.S.C. §112, first paragraph.

The Office Action acknowledges Applicants' claim for domestic priority under 35 U.S.C. § 119 (e) to provisional application No. 60/203,151, filed May 9, 2000. However, the Action fails to recognize that the instant application is entitled to claim priority to the earlier-filed provisional application, because the Action asserts that the provisional application fails to provide adequate support under 35 U.S.C. § 112, first paragraph for claims 1-7, 13-19, and 25-34.

The subject matter of pending claims as amended relates to methods for identifying compounds that improve wound healing in a diabetic animal, wherein the method may act as a surrogate for identifying compounds that improve diabetic neuropathy or neurological disorders associated with diabetes. Applicants were the first to recognize that drugs that improve diabetic neuropathy also improve wound healing in diabetics, and this disclosure was contained, *inter alia*, in their provisional application, for example, on page 1, lines 1-3 of the disclosure: "We hypothesi[ze] that the drug designated as 676 [an aldose reductase inhibitor] and currently in phase I human trials to treat complications of diabetes may lead to improved wound healing in diabetic subjects by improving cutaneous neurologic function." The correlation between diabetic neuropathy and wound healing in a diabetic subject is further affirmed in the disclosure of the provisional application, for example, on page 1, last sentence of the third paragraph: "These studies are consistent with *our hypothesis* that decreased innervation in the skin contributes to the failure of wound healing" (*emphasis added*). Wound healing is thereafter proposed as a model system for studying diabetic neuropathy, for example, on page 2, lines 7-8 of the 1st paragraph: "...these mice [db/db mice] provide a good model system for studying the role of decreased innervation in the setting of wound healing"; and the diabetic wound healing model: "...may be a fast and reliable method of assessing diabetic nerve function." (page 3, lines 2-3 of *Future Studies*)

The subject matter of all pending claims of this application encompass methods for identifying compounds that improve wound healing in a diabetic animal, wherein the

method may act as a surrogate for identifying compounds that improve diabetic neuropathy or neurological disorders associated with diabetes. These methods were explicitly disclosed in the provisional application, which disclosure would be recognized by persons of ordinary skill. Applicants respectfully contend that the claimed subject matter is supported by the provisional application No. 60/203,151, and thus it is entitled to the effective filing date of May 9, 2000.

B. The amended claims fulfill the requirements of 35 U.S.C. §112, second paragraph

Claims 1-7, 13-19, and 25-34 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office Action asserts that the terms “more rapidly,” “more completely,” or “less painfully” in Claims 1 and 13 as relative terms and thus indefinite. The mere fact that a term or phrase used in the claim may not have an absolutely precise meaning does not necessarily render the claim indefinite under 35 U.S.C. §112, second paragraph (M.P.E.P. §2173.05(b)). Applicants respectfully submit that the terms “more rapidly”, “more completely”, or “less painfully” are well within the grasp of one of skill in the art, especially where, as here, the terms are not used in a vacuum, but with regard to the degree of wound healing compared between a wound treated in the presence of a test compound and a control wound treated in the absence of the test compound. In addition, the specification provides detailed instructions concerning how to measure wound healing, *for example*, on page 14, lines 24-26. Thus Applicants respectfully submit that claims 1 and 13 are not indefinite when read in light of the specification, and respectfully request withdrawal of rejection on these grounds.

The Office Action also asserts that there is insufficient antecedent basis for the limitation “the human” in Claims 5, 13, 27, and 32; it appears that this recitation may contain a typographical error, and that Claims 5, 17, 27, and 32 were intended to be rejected on these grounds. Since Claims 5, 17, 27 and 32 have been canceled, this ground of rejection is now moot, and Applicants request that it be withdrawn.

Finally, the Office Action asserted that step (c) of Claims 1 and 13 is confusing. Applicants have amended these claims in response to this rejection, and submit that the

rejection is overcome by their amendment. Applicants respectfully request the Examiner to withdraw this ground of rejection

Applicants respectfully contend that they have overcome by amendment or traversed by argument all grounds of rejection based on 35 U.S.C. §112, second paragraph, they request that the Examiner withdraw these rejections.

C. The amended claims are not anticipated under 35 U.S.C. §102

Claims 1, 3-4, and 6-7 stand rejected under 35 U.S.C. §102(b) as being anticipated by Wong *et al.*, U.S. Patent No. 6,001,357. The Office Action asserts that Wong *et al.* disclose animal models of assessing the efficacy of a drug in treating skin wound.

Applicants respectfully traverse the rejection. Currently pending Claims 1, 3, 4, and 6-7 recite a method for identifying a compound that improves treatment of wounds to skin or another external body surfaces in a diabetic animal, comprising (a) producing a wound in the skin or another external surface of the animal; (b) permitting the wound to heal in the absence of a test compound, or treating the wound with a test compound; (c) comparing wound healing in the presence of the compound to wound healing in the absence of the compound; and (d) identifying the compound that improves treatment of wounds to skin or another external body surfaces in an animal. Wong *et al.* do not teach or suggest a method for identifying a compound that improves wound healing in a diabetic animal. Because Wong *et al.* does not teach or suggest all claim limitations of pending Claims 1, 3-4, and 6-7, the reference cannot anticipate Applicants' claimed invention. Applicants request that the Examiner withdraw this ground of rejection.

Claims 1, 3-4, and 6-7 stand rejected under 35 U.S.C. §102(b) as being anticipated by Chen *et al.* U.S. Patent No. 6,232,341 ('341 patent). The Office Action asserts that Chen discloses methods of assessing the efficacy of topical therapeutic preparation in treating a skin wound.

Applicants respectfully traverse the rejection. As an initial matter, the '341 patent issued on May 15, 2001, which is after the effective filing date (May 9, 2000) or the

actual filing date (May 9, 2001) of the instant application. The cited reference is thus not prior art under 35 U.S.C. §102(b).

Because the reference may be prior art under 35 U.S.C. §102(e), Applicants further address additional, substantive reasons why this reference does not anticipate the instantly-pending claims. Pending claims 1, 3, 4, and 6-7 recite a method for identifying a compound that improves treatment of wounds to skin or another external body surfaces in a diabetic animal. Chen *et al.* do not teach or suggest a method for identifying a compound that improves wound healing in a diabetic animal. Indeed, the Chen reference is limited to disclosure regarding methods for using specific compounds for wound healing. The disclosure relevant to Applicants' claims (col. 5, lines 1-41) concerns burning animal flesh, and not producing other types of skin wounds, such as puncture wounds which are particularly important to heal in diabetics (lest they become seriously infected).

Applicants respectfully contend that the Chen reference not teach or suggest a method for identifying a compound that improves wound healing in a diabetic animal. does not teach or suggest all claim limitations of pending Claims 1, 3-4, and 6-7, the reference cannot anticipate Applicants' claimed invention. Applicants request that the Examiner withdraw this ground of rejection.

Applicants respectfully contend that they have overcome by amendment or traversed by argument all grounds of rejection based on 35 U.S.C. §102. They therefore request that the Examiner withdraw these rejections.

D. The amended claims are not obvious under 35 U.S.C. §103

Claims 1-7, 13-19, and 25-34 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Chen *et al.* (Chen) in view of Jones *et al.* (WO 99/50268, Jones) and Spence (US Patent 4,226,232).

Specifically, the Action asserted that it would have been obvious to one of skill in the art to use an aldose reductase inhibitor (ARI) for comparative assessment of therapeutic efficacy of other agents; and assessing therapeutic efficacy of drugs in treating skin wound would require the same method steps for any skin etiology including

those caused by diabetes. Applicants respectfully traverse the rejection with the following argument.

Initially, the instantly-claimed invention provides a method for identifying a compound that improves wound healing in a diabetic animal (the subject matter of independent Claim 1), wherein the method may be used to identify compounds that improve diabetic neuropathy or neurological disorders associated with diabetes (the subject matter of independent Claim 13). The assertion of obviousness relying on the teachings of the Jones reference relating to ARIs therefore properly applies only to dependent Claims 2 and 14.

Regarding independent claims 1 and 13, and claims dependent thereupon, the Chen reference does not teach, suggest or motivate one of ordinary skill in the art to develop methods for identifying compounds that promote wound healing in a diabetic animal. The Spence reference does not cure these deficiencies. (Although the Action admits that the Spence reference is cited merely to show “general knowledge” in the art, Applicants fail to understand the relevance of a reference to a wound dressing to their inventive methods.) Similarly, the Jones reference, while disclosing aldose reductase inhibitors, does not teach or suggest any relationship between these molecules and wound healing, or contain any teaching that would motivate one of ordinary skill to develop methods for investigating the relationship between ARIs and wound healing. Indeed, the portion of the reference cited in the Action relates to sorbitol accumulation in sciatic nerve, and makes no mention and has nothing to do with wound healing.

Moreover, the pending claims are not directed to wound healing in general, but wound healing in a diabetic animal. It was well known in the art at the time of the invention was made that diabetic wounds are significantly different from non-diabetic wounds. For example, diabetic wounds heal more slowly, have decreased innervation in the epidermis, and can often result in significant morbidity (page 1, line 20 to page 2, line 22 of Applicants’ specification). Accordingly, one of skill in the art would recognize these unique properties and characteristics of diabetic wounds, and would recognize that generic disclosure related to wound healing in the prior art would not be sufficient to raise a *prima facie* obviousness determination against Applicants’ claims directed specifically to wound healing in a diabetic animal.

Furthermore, even though the Jones reference relates to diabetic neuropathy, the reference is devoid of any mention of wound healing in diabetic animals. The reference neither teaches nor suggests any relationship between neuropathy and wound healing in diabetic animals. One skilled in the art would not have been motivated to combine or modify the cited references, or have a reasonable expectation of success of achieving the invention claimed in claim 13 if the references were so combined, because the relationship between wound healing and neuropathy in diabetic animals was not known in the prior art. Applicants respectfully contend that it would not have been obvious to one of skill in the art the claimed invention of independent Claims 1 and 13, as well as dependent claims thereon, in view of the teachings of the cited prior art, what was lacking in those teachings, and their argument set forth herein.

With respect to the assertion of obviousness for the methods of claims 2 and 14, wherein the test compounds are explicitly recited as ARIs, the finding that compounds such as ARI that are effective in improving diabetic neuropathy are also effective in promoting wound healing in diabetic animals was unexpected, not having been known in the prior art. Applicants thus respectfully contend that the invention claimed in claim 2 and 14 would not have been obvious to one of ordinary skill in the art at the time the invention was made in view of the cited references. The Jones reference, the only reference that teaches ARIs whatsoever, discloses the effects of the disclosed ARIs on diabetic cataracts, retinopathy and neuropathy. Jones is significantly silent on *any* effect whatsoever of ARIs on diabetic wound healing. The effects of ARI on diabetic wound healing, and hence the use of ARI as positive control in assessing the effect of other therapeutic agents on diabetic wound healing is not taught or suggested in any cited references, taken alone or in combination. The only place the relationship between compounds such as ARIs that are effective against diabetic neuropathy and wound healing comes from Applicants' own disclosure, which is unavailable against the instant claims. Applicants respectfully submit that the cited art could only (improperly) be considered to support a *prima facie* obviousness determination if there own teachings were used in a hindsight reconstruction of their invention, which of course is impermissible. Applicants respectfully contend that the prior art, limited to what it does

and does not teach, does not support rejection of any of the rejected claims under 35 U.S.C. §103(a).

Based on the foregoing, Applicants respectfully contend that the asserted obviousness rejection has been traversed by their argument and respectfully request that the Examiner withdraw these grounds of rejection.

CONCLUSIONS

It is believed that all requirements of patentability are fully met, and allowance of the claims is respectfully requested.

If the Examiner believes it to be helpful, the Examiner is invited to contact the undersigned attorney by telephone at (312) 913-0001.

Respectfully submitted,
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